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10/518,759	12/21/2004	Takekuni Nakama	58777.000017	2877

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EXAMINER	
HISSONG, BRUCE D	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 05/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/518,759	NAKAMA, TAKEKUNI	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 December 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/24/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A. Formal Matters

1. The contents of the instant application, including the specification, figures, and amended claims, received on 12/21/2004, have been entered into the record.

2. Claims 1-11 are currently pending and are the subject of this Office Action.

B. Information Disclosure Statement

The information disclosure statement received on 12/21/2004 has been fully considered by the Examiner.

C. Claim Objections

1. The Examiner suggests the syntax of claim 1 can be improved by amending the claim to read "An agent for treatment of pemphigoid, with said agent comprising interferon-γ as an active ingredient." Furthermore, claims 2-8 are objected to for depending from claim 1.

2. The Examiner notes that claim 6 further limits the subject matter of claim 5, and therefore suggests that claim 6 should be amended so that it depends from claim 5 instead of claim 1.

D. Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an agent for treatment of bullous pemphigoid comprising

the interferon (IFN)-γ used in the clinical case examples, does not reasonably provide enablement for an agent for treatment of any other type of pemphigoid, and comprising all other types of IFN-γ. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breath of claims. Ex Parte Forman, (230 USPQ 546 (Bd. Pat. App. & Int. 1986); In re Wands, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The breadth of the claims is excessive because the claims are drawn to an agent comprised of any type of IFN-γ, from any source or species. The specification, on page 6, line 23 – p. 7, line3, teaches that the IFN-γ used in the present invention may be any natural or recombinant IFN-γ, and specifically recites IFN-γ1a, -γ1b, and –γn1. However, the specification does not teach, or provide examples showing that any other IFN-γ, such as IFN-γ from other species, could be used in the present invention. It is known in the art that the human and mouse species share only limited homology (40%) and also share no significant cross-species activity (Fitzgerald *et al*, The cytokine facts book, 2nd Ed. 2001, p. 322-327). A person of ordinary skill in the art would not be able to predict the effect of any non-human IFN-γ, or any other IFN-γ other than the IFN-γ used in the clinical examples of the instant specification, on a human patient with bullous pemphigoid without further, undue experimentation. Furthermore, the claims read on an agent for the treatment of any type of pemphoigoid. The specification provides examples of an agent for the treatment of bullous pemphigoid, but does not provide guidance or examples showing that any other type of pemphigoid can be treated by the claimed agent, and a person of ordinary skill in the art would not be able to predict the effect of any type of IFN-γ on multiple diseases having different symptoms and underlying causes.

In summary, the breadth of the claims is excessive because they read on an agent for treatment of any type of pemphigoid, with said agent comprising any IFN-γ molecule from any source or species. The specification lacks guidance and examples which show that any IFN-γ other than that used in the clinical case examples section can be used to treat any type of pemphigoid except bullous pemphigoid, and the relevant art suggests unpredictibility regarding

whether or not an IFN-γ molecule from any species or source could be used as claimed, and whether any type of pemphigoid other than bullous pemphigoid could be treated by the claimed agent. Therefore, a person of ordinary skill in the art would require further, undue experimentation to make and use an agent for treatment of any type of pemphigoid, except bullous pemphigoid, comprised of any IFN-γ other than the IFN-γ used in the clinical examples section.

2. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an agent for treatment of pemphigoid comprising an IFN-γ mutant described on p. 7, lines 3-17 of the instant specification, does not reasonably provide enablement for an agent for treatment of pemphigoid comprising any other IFN-γ mutant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The breadth of the claim is excessive because it does not define or place any limitations on possible IFN-γ mutations, other than that they must treat any type of pemphigoid, and thus the claim is drawn to an unreasonably large number of molecules. Although the specification teaches that the IFN-γ mutants listed on p. 7, lines 3-17 can be used in the claimed agent for treatment of pemphigoid, there is no guidance of examples in the specification that teach that any other possible IFN-γ could be used. A person of ordinary skill in the art would not be able to predict which of the many possible amino acids could be deleted or replaced and still result in an IFN-γ molecule that could be used commensurate in scope with the claims. Because the claim does not limit the nature of the mutations, it would clearly be an undue burden on a skilled artisan to create all possible IFN-γ mutations, and then test them for the ability to treat pemphigoid as claimed. It would require significant and excessive experimentation on the part of the skilled artisan to make and test each possible IFN-γ mutant for the ability to treat any type of pemphigoid, and the standard of enablement requires a person of ordinary skill in the art to be able to "make and use" an invention, rather than "make and test".

Therefore, due to the excessive breadth of the claim, which reads on all possible IFN-γ mutants, the lack of guidance and examples in the specification teaching that any IFN-γ other than those disclosed on p. 7, lines 3-17, and the unpredictability inherent in the art regarding which of the many possible IFN-γ mutants could still be effective in treating pemphigoid, a

person of ordinary skill in the art would require further, undue experimentation to make and use an agent for treatment of pemphigoid commensurate in scope with the claim.

E. Claim Rejections - 35 USC § 112, first paragraph – written description

1. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is drawn to an agent for the treatment of pemphigoid comprising an IFN-γ mutant. Although the specification does describe some IFN-γ mutants (see enablement rejection 2 above), the claim reads broadly on any possible IFN-γ mutant. The specification and the claim do not define or limit the type of mutant, or require the IFN-γ mutant of the instant invention to have any particular structure. Thus, the Applicant has not adequately described the genus of IFN-γ mutants that can be used as an agent for the treatment of pemphigoid.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is that the active ingredient in the agent for treatment of pemphigoid be an IFN-γ mutant. There is no identification of any particular portion of the wild-type IFN-γ that must be conserved in order to maintain function. Accordingly, in the absence of sufficient distinguishing characteristics, the specification does not provide adequate written description of the claimed genus.

F. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims of the instant invention are drawn to an "agent" for treatment of pemphigoid comprising IFN-γ as an active ingredient. The intended meaning of the term "agent" is not clear, and is not defined by the claims or the specification. The term could be interpreted to mean a composition, a medical device for drug delivery (such as a syringe), or something else. Thus, the metes and bounds of the term "agent" are not clear. For the purpose of examination, the Examiner has interpreted the term "agent" to mean a composition.

2. Claims 2 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to an agent for treatment of pemphigoid comprising IFN-γ in a daily dose of 200,000 – 2,000,000 JRU (claim 2) or 2,000,000 JRU (claim 7). The acronym JRU should be spelled out the first time it is used in a claim. Furthermore, neither the specification or the claims define the term, or present a conversion from JRU to international units (IU). For the purpose of examination, the Examiner has assumed, in the absence of any other information, that 1JRU = 1 IU.

3. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is indefinite because the elements recited in the claim do not constitute proper Markush groups. The claims are indefinite in the alternative use of "and/or" because it is not clear what controls which of these limitations. See MPEP § 2173.05(h).

G. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed

in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 1-11 are rejected under 35 U.S.C. 102(b) as being anticipated by von Eichborn *et al* (US 5,145,677). The claims of the instant invention are drawn to an agent for treatment of pemphigoid comprising IFN-γ as an active ingredient. The claims are further drawn to an agent in a daily dose of 200,000 – 2,000,000 JRU, suitable for intravenous injection, and further comprising an antihistaminic, antiallergic, and/or a corticosteroid. The claims also recite a therapeutic composition comprising IFN-γ as an active ingredient, and methods for treating pemphigoid by administering the IFN-γ-containing composition.

von Eichborn *et al* teaches administration of IFN-γ compositions for treatment of a number of malignant, infectious, and autoimmune diseases (abstract; column 3, lines 3-16; column 5, line 42 – column 6, line 37; and claim 1). Also disclosed by von Eichborn *et al* is administration of IFN-γ in doses ranging between 0.1 – 2,000,000 IU (claim 1 - note that as stated above in the 35 U.S.C. 112, second paragraph rejection 2, in the absence of evidence to the contrary, the Examiner has assumed that 1 JRU – 1 IU), and administration of IFN-γ wherein the IFN-γ is natural IFN-γ, recombinant IFN-γ, and derivatives thereof (claim 2; column 3, lines 42-50). Furthermore, von Eichborn *et al* teaches intravenous administration (claim 5), and co-administration with other pharmaceutical reagents, including corticosteroids (column 7, lines 6-30; claim 8). Thus, by teaching compositions of IFN-γ, in doses that encompass the claimed doses of the instant application, and teaching administration by intravenous injection and with co-administration of corticosteroids, von Eichborn *et al* meets the limitations of claims 1-4 and 7 of the instant application. Furthermore, because the claimed IFN-γ mutants of the instant application can be the result of any type of addition, subtraction, or deletion of the wild-type molecule, any mutation would produce a "derivative" of the molecule. Therefore, the derivatives of IFN-γ taught by von Eichborn meet the limitations of claim 8 of the instant application, which read mutants of IFN-γ that could be interpreted by one of ordinary skill in the art as "derivatives" of IFN-γ.

Claims 5-6 and 9-11 of the instant application specifically recite treatment of pemphigoid, and methods of treating pemphigoid. Although von Eichborn *et al* does not specifically teach treatment of pemphigoid, it is noted that claims 5-6 and 9 of the instant application are drawn to a composition comprising IFN-γ rather than an actual method of treatment (see 35 U.S.C. 112, 2nd paragraph rejection 1 above), and that, as discussed in the preceding paragraph, von

Eichborn *et al* does teach compositions of IFN-γ. In the absence of any evidence to the contrary, the IFN-γ compositions of von Eichborn *et al* would be expected to be effective in treating various forms of pemphigoid. It should also be noted that because the Office does not have the facilities for testing the compositions of the prior art or the instant application, the burden is on the applicant to show a novel and unobvious difference between the claimed agent for treating pemphigoid and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.)." Therefore, von Eichborn *et al* meets the limitations of claims 5-6 and 9 of the instant application. Similarly, von Eichborn *et al* also meets the limitations of claims 10-11 of the instant application, which are drawn to methods of treating pemphigoid comprising administration to a patient a therapeutic composition of IFN-γ. Although the methods of the instant application and those taught by von Eichborn *et al* are not identical, they are not patentably distinct from each other because the process steps of administering compositions comprising IFN-γ are the same regardless of whether the purpose is to treat the malignant, infectious, or autoimmune diseases disclosed in von Eichborn *et al*, or treat pemphigoid as claimed in the instant application (Ex parte Novitski, 26 USPQ 1391). The instant process claims would inherently possess acetylcholine receptor synthesis stimulating activity.

2. Claims 1, 5-7, and 9-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Shachar *et al* (US 20030053985 A1). The subject matter and claim limitations of the instant invention have been discussed in the preceding rejection over von Eichborn *et al.* Shachar *et al* teach a method of treating inflammation in a subject by administration of IFN-γ (abstract, claim 1), and specifically recites bullous pemphigoid as a disease that can be treated by said administration of IFN-γ (paragraphs 0053 and 0240, as well as claims 23 and 87). Shachar *et al* also teach administration of IFN-γ in a pharmaceutical composition which includes a pharmaceutically acceptable carrier (paragraph 0094 and claim 64), and teaches dosage ranges for IFN-γ administered in the pharmaceutical compositions, including 1 - 8,000,000 IU. Because Shachar *et al* teaches pharmaceutical compositions of IFN-γ for the treatment of bullous pemphigoid, and methods of administering IFN-γ for said treatment, Shachar *et al* meets the limitations of claims 1, 5-6, and 9-10 of the instant application. Furthermore, as stated above in the 35 U.S.C. 112, second paragraph rejection 2, in the absence of evidence to the contrary, the Examiner has assumed that 1 JRU – 1 IU. Therefore, the dosage of claim 7 is

encompassed by the range taught by Shachar *et al*, the thus the limitations of claim 7 are also met.

H. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 2-4 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shachar *et al.* The claims of the instant application are drawn to an agent for treatment of pemphigoid comprising IFN-γ as an active ingredient, with said IFN-γ in a daily dose of 200,000 – 4,000,000 JRU, in a form suitable for intravenous injection, and in combination with an antihistaminic, antiallergic, and/or a corticosteroid. Shachar *et al* teach administration of pharmaceutical compositions of IFN-γ for treatment of inflammatory disease, and specifically teaches treatment of bullous pemphigoid. Shachar *et al* is silent regarding administration via intravenous injection, in a daily dose of 200,000 – 4,000,000 JRU, or co-administration of an antihistaminic, antiallergic, and/or a corticosteroid.

A person of ordinary skill in the art, however, would have been motivated to follow the teachings of Shachar *et al* to practice the instant invention commensurate in scope with the claims. Shachar *et al* teaches that administration of IFN-γ for treatment of inflammatory disease can be via several methods, including parenteral administration (paragraph 0095 and claim 65). Although Shachar *et al* does not specifically recite intravenous administration, a person of ordinary skill in the art would know that intravenous injection is a commonly known and practiced method of parenteral administration, and therefore would be motivated to administer the IFN-γ composition of Shachar *et al* via intravenous injection. Furthermore, administration of corticosteroids, antihistaminics, and/or antiallergics represents common and well-known methods of treating pemphigoid, as described on p. 2, lines15-28, of the instant specification, and combining two or more effective agents into one composition is also common and well-known in the art. Therefore, the skilled artisan, by virtue of knowing that antihistaminics, antiallergics, and/or corticosteroids can treat pemphigoid, would be motivated to co-administer

these compounds with the IFN-γ compositions of Shachar *et al.* It should be noted that the specification of the instant application is not being used in a grounds of rejection, but to merely point out what was already known in the art at the time the invention was conceived. Finally, although Shachar *et al* does not specifically teach administration of IFN-γ at doses of 200,000 – 4,000,000 JRU, a person of ordinary skill in the art would be motivated and able to optimize the dosage in order to obtain the most favorable clinical outcome. Such an optimization would be routine for a skilled artisan, and is a common component of the treatment of many diseases.

Therefore, by following the teachings of Shachar et al, a person of ordinary skill in the art would have both the motivation, and a reasonable expectation of success, in practicing the instant invention commensurate in scope with the claims.

I. Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D. whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BDH
Art Unit 1646

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